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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/920,491	07/31/2001	Shoulian Dong	3417	1435

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EXAMINER	
LU, FRANK WEI MIN	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 12/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/920,491	DONG, SHOULIAN	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 September 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20,22 and 24-47* is/are pending in the application.

4a) Of the above claim(s) *28,32,34,42,44,45 and 47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20,22,24-27,29-31,33,35-41,43 and 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election of Species

1. Applicant's election without traverse of species (1) (claims 27 and 31), species (4) (claim 43) and species (6) (claim 46) filed on September 5, 2003 is acknowledged. In view of applicant's election and the amendment filed on May 20, 2003, claims 22, 24, 25-27, 29-31, 33, 35-41, 43, and 46 will be examined.

2. This application contains claim 34 drawn to an invention nonelected filed on May 9, 2002. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Information Disclosure Statement

3. The examiner notes that previous examiner, David Gunter, signed 1449 Forms in Paper Nos: 3 and 6-8 in the office action mailed on January 15, 2003. However, the examiner only can find 1449 form filed on November 6, 2002 in this instant application.

Claim Objections

4. Claims 20, 25, 29, and 33 are objected to because of the following informalities: (1) "a first and second restriction enzyme" should be "a first and a second restriction enzyme"; and (2) "amplifying the fragments, wherein fragments that were" should be "amplifying the fragments, wherein the fragments that are".

5. Claims 20, 25, and 29 are objected to because of the following informality: "to be present on fragments that were cut on one end by the first restriction enzyme and on the other end by the

second restriction enzyme are enriched in the amplification product relative to the fragments that were" should be "to be presented on the fragments that are cut on one end by the first restriction enzyme and on the other end by the second restriction enzyme are enriched in the amplification product relative to the fragments that are".

6. Claim 24 is objected to because of the following informality: "polymorphisms predicted to be present on fragments that were" should be "the polymorphisms predicted to be present on the fragments that are".

7. Claims 25 and 29 are objected to because of the following informality: "polymorphisms" should be "polymorphism" in view of "polymorphism" in the preambles.

8. Claims 29 and 33 are objected to because of the following informality: "fragmenting the nucleic acid sample" should be "fragmenting the first nucleic acid sample".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 20, 22, 24-27, 29-31, 35-39, 41, 43, and 46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claims 20, 25, 29, and 33 recite the limitation "the same restriction enzyme" in the claims. It is unclear that "the same restriction enzyme" means a fist restriction enzyme or a second restriction enzyme recited in the claims. Please clarify.

12. Claim 20 is rejected as vague and indefinite in view of the phrase "the alleles present at polymorphisms". Since an allele is much boarder than polymorphism, it is impossible that an allele is presented at polymorphisms. The correct way is that polymorphisms are presented at an allele. Please clarify.

13. Claims 25 and 29 are rejected as vague and indefinite in view of the phrase "the alleles present at polymorphisms" in preamble and the method steps. Since an allele is much boarder than polymorphism, it is impossible that an allele is presented at polymorphisms. The correct way is that polymorphisms are presented at an allele. Please clarify.

14. Claim 33 is rejected as vague and indefinite in view of the phrase "the presence or absence of one or more alleles of one or more polymorphisms". Since an allele is much boarder than polymorphism, it is impossible that an allele is presented at polymorphisms. The correct way is that polymorphisms are presented at an allele. Please clarify.

15. Claims 35-39 recite the limitation "the first nucleic acid sample" in the claims. Since the first nucleic acid sample recited in claims 35-39 contains fragments digested by the first and the second restriction enzymes, the first nucleic acid sample recited in claims 35-39 appear to be different from the nucleic acid sample recited in claim 20. Therefore, "the first nucleic acid sample" lacks sufficient antecedent basis. Please clarify.

16. Claim 41 recites the limitation "each adaptor" in the claims. Since claim 20 does not recite two adaptors, "each adaptor" lacks sufficient antecedent basis. Please clarify.

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

18. Claims 20, 24-27, 33, and 40 are rejected under 35 U.S.C. 102(e) as being anticipated by Macasky Feazel *et al.*, (US Patent No. 6,100,030, filed on January 1998, priority date: January 1997).

Regarding claims 20 and 25, Macasky Feazel *et al.*, teach method of mapping a polymorphic genetic marker, comprising the steps of: (i) providing a mixture of restriction enzyme-digested nucleic acids from biological samples; (ii) amplifying the mixture of restriction enzyme-digested nucleic acids; (iii) identifying a set of differentially amplified nucleic acids in the mixture; and, (iv) mapping at least one of the differentially amplified nucleic acids to a unique genetic polymorphism, thereby providing a marker for the polymorphism (see column 54, claim 15). Since Macasky Feazel *et al.*, teach providing a mixture of restriction enzyme digested nucleic acid from biological samples by double digestion of the nucleic acid with EcoR I and Mse I, ligating the mixture of restriction enzyme digested nucleic acid with an EcoR I adapter and a Mse I adapter and amplifying the ligation product of digested nucleic acids (see Figure 1 and claim 15 in column 54), Macasky Feazel *et al.*, disclose fragmenting a nucleic acid sample using a first and a second restriction enzyme to produce fragments, ligating adaptors to the fragments and amplifying the fragment as recited in claims 20 and 25. Based on EcoR

I/Mse I double digestion, digested nucleic acids taught by Macasky Feazel *et al.,* comprise three types: (1) EcoR I digested nucleic acids (both ends with EcoR I cutting sites); (2) Mse I digested nucleic acids (both ends with Mse I cutting sites); and (3) EcoR I/ Mse I digested nucleic acids (one end with an EcoR I cutting site and another end with a Mse I cutting site). Since, as shown in Figure 1, one end of the ligated product has an EcoR I adapter while another end of the ligated product has a Mse I adapter and the adapters are required for annealing primers to the ligated digested nucleic acids, the most amplified product are fragments that are cut on one end by the first restriction enzyme (ie., EcoRI) and on the other end by the second restriction enzyme (ie., Mse I). Therefore, Macasky Feazel *et al.,* disclose fragments that are cut on one end by the first restriction enzyme (ie., EcoRI) and on the other end by the second restriction enzyme (ie., Mse I) are enriched in the amplification product relative to the fragments that were cut on both ends by the same restriction enzyme (ie., EcoRI or Mse I) as recited in claims 20 and 25. Since Macasky Feazel *et al.,* teach an array of selection probes comprising polymorphic nucleotides and mapping polymorphic genetic marker or selection of polymorphic variants from the nucleic acid sample by hybridizing the amplified ligated products to the array (see claim 9 in claim 53, claim 15 in column 54, claims 24 and 32 in column 32, and claim 47 in column 56), Macasky Feazel *et al.,* disclose providing a nucleic acid array consisting essentially of probes designed to detect polymorphisms predicted to be presented on the fragments that are cut on one end by the first restriction enzyme and on the other end by the second restriction enzyme, hybridizing the amplified fragments to the array, and analyzing a hybridization pattern resulting from the hybridization or generating a hybridization pattern resulting from the hybridization or/and

determining the polymorphisms in the individual based upon an analysis of the hybridization pattern as recited in claims 20 and 25.

Regarding claim 24, since Macasky Feazel *et al.,* teach to hybridize probes to amplification mixture and scan image of hybridization signal (see Figure 11), claim 24 is anticipated by Macasky Feazel *et al.*.

Regarding claims 26 and 27, since the phrase "polymorphisms predicted to be presented" in claim 25 indicates that polymorphisms is not required for the fragment recited claim 25 and claims 25 and 26 are dependent on claim 25, the limitations recited in claims 26 and 27 are mean less.

Regarding claim 33, since Macasky Feazel *et al.,* teach providing a mixture of restriction enzyme digested nucleic acid from biological samples by double digestion of the nucleic acid with EcoR I and Mse I, ligating the mixture of restriction enzyme digested nucleic acid with an EcoR I adapter and a Mse I adapter and amplifying the ligation product of digested nucleic acids (see Figure 1 and claim 15 in column 54), the nucleic acid and the amplified product are a first nucleic acid and a second nucleic acid sample as recited in claim 29. Since claim 29 and claim 22 have the same method steps, claim 29 is anticipated by Macasky Feazel *et al.*.

Regarding claim 40, since Macasky Feazel *et al.,* teach that the nucleic acid sample is cDNA or genomic DNA (see claim 17 in column 54), claim 40 is anticipated by Macasky Feazel *et al.*.

Therefore, Macasky Feazel *et al.,* teach all limitations recited in claims 20, 24-27, 33, and 40.

Claim Rejections - 35 USC § 103

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. Claim 29-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Macasky Feazel *et al.*, (1997) as applied to claims 20, 24-27, 33, and 40 above, and further in view of Guire *et al.*, (US Patent No. 6,514,768 B1, filed on January 1999).

The teachings of Macasky Feazel *et al.*, have been summarized previously, *supra.* Since Macasky Feazel *et al.*, teach providing a mixture of restriction enzyme-digested nucleic acids from biological samples (see Figure 1 and claim 15 in column 54), Macasky Feazel *et al.*, disclose providing a first nucleic acid sample from each of the individuals as recited in claim 29 wherein the biological samples taught Macasky Feazel *et al.*, have two or more individuals. Except providing a plurality of identical nucleic acid arrays, claims 29 and 33 have the same method steps.

Regarding claims 30 and 31, since the phrase "polymorphisms predicted to be presented" in claim 29 indicates that polymorphisms is not required for the fragment recited claim 29 and claims 30 and 31 are dependent on claim 25, the limitations recited in claims 30 and 31 are mean less.

Macasky Feazel *et al.*, do not teach to provide a plurality of identical nucleic acid arrays as recited in claim 29.

Guire *et al.*, teach replicable probe array. A plurality of identical nucleic acid arrays are made by a master nucleic acid array (see abstract, columns 3, and column 18, lines 42-53).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have provided a plurality of identical nucleic acid arrays during the process of practicing the method recited in claim 33 in view of the patents of Macasky Feazel *et al.*, and Guire *et al.*. One having ordinary skill in the art would have been motivated to do so because Guire *et al.*, have successfully produced a plurality of identical nucleic acid arrays from a master nucleic acid array and the availability of a plurality of identical nucleic acid arrays in a hybridization assay would let one having ordinary skill in the art at the time the invention was made to use the identical array for different purposes and save his or her time for making a nucleic acid array. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to make a plurality of identical nucleic acid arrays during the process of practicing the method recited in claim 33.

21. Claim 41 is rejected under 35 U.S.C. 103(a) as being unpatentable over Macasky Feazel *et al.*, (1997) as applied to claims 20, 24, 25, 29, and 40 above, and further in view of Makarov *et al.*, (US Patent No. 6,197, 557, filed on September, 1998).

The teachings of Macasky Feazel *et al.*, have been summarized previously, *supra.*

Macasky Feazel *et al.*, do not disclose that ligation of one strand of an adaptor to the fragments is blocked as recited in claim 41.

Makarov *et al.*, teach to ligate a 3'-blocked oligonucleotide adaptor to a double stranded DNA molecule (see column 89 and Figures 30A and 30B).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 20 using a 3'-blocked oligonucleotide adaptor in view of the patents of Macasky Feazel *et al.*, and Makarov *et al.*. One having ordinary skill in the art would have been motivated to do so because Makarov *et al.*., have successfully used a 3'-blocked oligonucleotide adaptor in a ligation reaction and the simple replacement of one kind of adaptor (i.e., 3'-unblocked oligonucleotide adaptor taught by Macasky Feazel *et al.*,) from another kind of adaptor (i.e., 3'-blocked oligonucleotide adaptor taught by Makarov *et al.*.,) during the process of the ligation reaction as recited in claim 20 would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because the replacement would not change the experimental results.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

22. Claims 41, 43, and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Macasky Feazel *et al.*, (1997) as applied to claims 20, 24, 25, 29, and 40 above, and further in view of Su *et al.*, (US Patent No. 6,632, 661, filed on July 20, 2001).

Since parent case 09/428,350 (now US Patent No. 6,261,947) does not have the limitation recited in claims 41, 43, and 46, priority date for claims 41, 43, and 46 in this instant application is considered as its filing date (July 31, 2001).

The teachings of Macasky Feazel *et al.,* have been summarized previously, *supra.*

Macasky Feazel *et al.,* do not disclose that ligation of one strand of an adaptor to the fragments is blocked as recited in claim 41, that ligation is blocked by the absence of a phosphate at the 5' end of an adaptor strand as recited in claim 43, and that ligation is blocked at the 5' end of one strand of one adaptor and at the 3' end of one strand of the other adaptor as recited in claim 46.

Su *et al.,* teach to ligate a 3'-blocked oligonucleotide adaptor and a 5'-blocked oligonucleotide adaptor (absence of a phosphate from 5' end of an adaptor) to a double stranded DNA molecule (see column 8, lines 38-61 and Figures 1A and 5).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 20 using a 3'-blocked oligonucleotide adaptor in view of the patents of Macasky Feazel *et al.,* and Makarov *et al.*. One having ordinary skill in the art would have been motivated to do so because Su *et al..,* have successfully used a 3'-blocked oligonucleotide adaptor and a 5'-blocked oligonucleotide adaptor (absence of a phosphate from 5' end of an adaptor) in a ligation reaction and the simple replacement of one kind of adaptor (i.e., unblocked oligonucleotide adaptor taught by Macasky Feazel *et al.,*) from another kind of adaptor (i.e., blocked oligonucleotide adaptor taught by Su *et al..,*) during the process of the ligation reaction as recited in claim 20 would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill

in the art at the time the invention was made because the replacement would not change the experimental results.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

Conclusion

23. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

24. No claim is allowed.

25. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270 (before January 13, 2004) or 571-272-0746 (after January 13, 2004). The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
PSA
December 12, 2003

GARY BENZION, PH.D
SUPERVISORY PATENT EXAMINER
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